BIOGRAPHICAL SKETCH

NAME: Daniela Cesana
Unique identifier(s): https://orcid.org/0000-0001-6366-4224
Scopus Author ID: 14013948200
ResearcherID: AAN-4788-2020

POSITION TITLE: Group Leader

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Milan, Milan	MS	07/2003	Medical Biotechnologies
San Raffaele Telethon Institute for Gene Therapy, SR-Tiget, Milan, Italy	Predoctoral fellow	12/2005	Gene and cell therapy
San Raffaele Vita-Salute University, Milan, Italy & The Open University, London, UK	PhD	10/2010	Cellular and Molecular Biology
SR-Tiget, Milan, Italy	Postdoctoral Fellow	10/2019	Cellular and molecular Biology
SR-Tiget, Milan, Italy	Project leader	10/2023	Molecular biology, hematology
SR-Tiget, Milan, Italy	Program Leader	12/2024	Gene and cellular therapy, hematology

A. Personal Statement

(Here you can insert a short description of your professional status and achievements. Max 10 lines)

I am a molecular biologist with over 15 years of experience in gene therapy, focused on translating molecular insights into clinically relevant innovations. My early work at SR-Tiget contributed to the development of safer viral vectors and to understanding insertional mutagenesis, supporting next-generation gene therapies. Over time, my research has shifted toward technology development, leading to the creation of LiBIS-seq, a patented cfDNA-based method for non-invasive monitoring of engineered cells in vivo.I currently lead the Tissue Dynamics and Biomarker Signature Discovery Unit at SR-Tiget, where we develop cfDNA-based approaches to capture the spatiotemporal dynamics of biological responses to gene and cell therapies. By integrating genomic, epigenetic, and transcriptomic signals, we aim to decode interactions between therapeutic cells and host tissues across diseases.Our goal is to establish cfDNA as a real-time, non-invasive biomarker platform to monitor efficacy, detect toxicity, and anticipate resistance or relapse. We apply this strategy across gene therapy, CAR-T, oncology, and immune-mediated diseases. In parallel, we leverage computational and AI-driven approaches to extract actionable insights, advancing more predictive and personalized therapeutic strategies.

B. Positions and Honors

Positions and Employment

(Complete the following table. Begin with older positions. Add/delete rows as necessary.)

date1- date2	*Position*
2003-2006	Graduate Fellow at SR-Tiget, Safety of Gene Therapy and Insertional

	Mutagenesis Unit, Naldini Lab, IRCCS, San Raffaele Hospital, Milan, Italy.
2006-2010	Ph.D. student in Cellular and Molecular Biology at SR-Tiget, Vita-Salute San Raffaele University, IRCCS, San Raffaele Hospital, Milan, Italy. Director of Studies: Prof. Luigi Naldini
2010- 2016	Postdoctoral fellow at SR-Tiget, Safety of Gene Therapy and Insertional Mutagenesis Unit, IRCCS, San Raffaele Hospital, Milan, Italy. Supervisor: Dr. Eugenio Montini
2016- 2019	Senior Postdoctoral fellow at SR-Tiget, Safety of Gene Therapy and Insertional Mutagenesis Unit, IRCCS, San Raffaele Hospital, Milan, Italy. Supervisor: Dr. Eugenio Montini
2019-2023	Project Leader at SR-Tiget, Safety of Gene Therapy and Insertional Mutagenesis Unit, IRCCS San Raffaele Hospital, Milan, Italy, Supervisor: Dr. Eugenio Montini
2023-2024	Program Leader at SR-Tiget, IRCCS, San Raffaele Hospital, Milan, Italy.
01/2025 –Today	Group Leader at the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget), Tissue dynamics and biomarker signature discovery unit, IRCCS, San Raffaele Hospital, Milan, Italy

Honors

(Complete the following table, Add/delete rows if necessary.)

date1	*honour*
2019	Recipient of the Excellence in Research Award for Students and Fellows at American Society for Cell and Gene Therapy (ASGCT), Washington, USA, May 2019
2023	National Scientific qualification as second-level professor for - Molecular Biology- Academic Recruitment Field 05/E, and Genetics- Academic Recruitment Field 05/I
2022	Meritorious Abstract Travel Award - ASGCT-Washington, DC (USA)
2021	Meritorious Abstract Travel Award - ASGCT-Virtual
2017	Meritorious Abstract Travel Award - ASGCT- Washington, DC (USA)
2016	Meritorious Abstract Travel Award - ASGCT-Washington, DC (USA)
2015	Meritorious Abstract Travel Award - ASGCT- New Orleans, LA (USA)
2015	Outstanding Poster Presentation Award- ASGCT- New Orleans, LA (USA)
2012	Meritorious Abstract Travel Award -ASGCT- Philadelphia, PA (USA)
2010	Meritorious Abstract Travel Award -ASGCT-Washington, DC (USA)

Patent

Application date	*Application Number*
2020	Name of the invention: Method for Analyzing Insertion Sites (LIBIS-seq) Inventor(s): Daniela Cesana and Eugenio Montini Owner(s): IRCCS Ospedale San Raffaele and Fondazione Telethon Country patent number Europe (EP3953490), patent application pending in USA (US2023159985), and Canada (CA3136532)
2024	Name of the invention: Polynucleotides (vector backbones with enhanced safety profile) Inventor(s): Daniela Cesana, Eugenio Montini and Monica Volpin Owner(s): Ospedale San Raffaele S.r.l. and Fondazione Telethon ETS Country patent number: International Patent Application N. PCT/EP2024/080150 (pending)

Reviewer Experience

(List the journals where you have acted as reviewer.)

Molecular Therapy, Journal of Virology, Plos one, Human Gene Therapy, Frontiers, Clinical Epigenetics, Human Genomics

C. Contributions to Science

(Here you can insert a short description of your contributions to science (max 20 lines) followed by the list of the 10 most significant publications of the last 10 yrs)

My research has consistently focused on the molecular mechanisms regulating genomic function in health and disease, with a particular emphasis on gene therapy (GT). After joining SR-Tiget, I contributed to early studies demonstrating both the therapeutic potential and risks of γ-retroviral (γRV) vectors. I helped establish the first in vivo tumor-prone mouse model revealing γRV-associated oncogenicity and the improved safety of lentiviral vectors (LV). During my PhD, I dissected the interaction between retroviral vector regulatory elements and the host genome, demonstrating that γRV genotoxicity is driven by active LTRs and promoter-targeting bias. As a postdoc, I showed that even self-inactivating LV vectors can alter host gene transcription through aberrant chimeric transcripts, and later confirmed this mechanism in vivo. Upon obtaining independent funding, I demonstrated that HIV-1 integration can modulate host gene expression to support persistence in T regulatory cells. I then developed and patented LiBIS-Seq, a liquid biopsy-based method to track vector integration sites from cfDNA, enabling non-invasive clonal monitoring in GT patients. As project leader, I established platforms and computational tools for AAV integration site analysis. This work revealed a novel targeting mechanism of AAV vectors at RAG-induced DNA breaks in TCR loci, enabling stable gene transfer without conditioning, while also identifying safety risks in gene editing contexts due to integration at nuclease-induced breaks. More recently, I reported the first case of GT-related T-ALL in an ADA-SCID patient treated with γRV vectors. In parallel, I developed expertise in statistical and computational analysis of large-scale genomic data. Currently, I lead a research program at SR-Tiget focused on developing cfDNA-based approaches to characterize the spatiotemporal dynamics of biological processes in GT patients, to predict and tailor therapeutic efficacy.

1. *Carlo Cipriani, Laura Rudilosso, Dhwanil A. Dalwadi, Marco Masseroli, Markus Grompe, Eugenio Montini, Andrea Calabria, Daniela Cesana.* **"**RAAVioli: A Comprehensive Approach to Characterizing AAV Vector Integrations and Rearrangements". ***2026, Molecular Therapy Advances, doi: 10.1016/j.omta.2025.201659***

2. Calabria A, Spinozzi G, Cesana D, Buscaroli E, Benedicenti F, Pais G, Gazzo F, Scala S, Lidonnici MR, Scaramuzza S, Albertini A, Esposito S, Tucci F, Canarutto D, Omrani M, De Mattia F, Dionisio F, Giannelli S, Marktel S, Fumagalli F, Calbi V, Cenciarelli S, Ferrua F, Gentner B, Caravagna G, Ciceri F, Naldini L, Ferrari G, Aiuti A, Montini E. "*Long-term lineage commitment in haematopoietic stem cell gene therapy*". ***2024, Nature. 2024 Dec;636(8041):162-171. doi: 10.1038/s41586-024-08250-x. PMID: 39442556***

3. Cesana D., Cicalese MP, Migliavacca M., Caruso R., Calabria A., Barzaghi F., Dionisio F., Giannelli S., Spinozzi G., Benedicenti F, Rudilosso L., Ciolfi A., Bruselles A., Pizzi S., Casiraghi M., Fossati C., Zancan S., Gabaldo M., Tucci F., Strocchio L., Bernardo M.E., Vinti L., Ferrua F., Calbi V., Gallo V., Carlucci F., Guerra A., Richardson A., Kudari M., Jones R., Cancrini C., Ciceri F., Naldini L., Tartaglia M., Montini E., Locatelli F. and Aiuti A. *"A case of T-cell acute lymphoblastic leukemia in retroviral gene therapy for ADA-SCID".* ***2024, Nature Communication, 2024 Apr 30;15(1):3662. doi: 10.1038/s41467-024-47866-5***

4. Calabria A., Cipriani C, Spinozzi G., Pouzolles M., Esposito S., Benedicenti F., Taylor N., Zimmermann V.S., Montini E., **Cesana D.** *"Intrathymic AAV delivery results in therapeutic site-specific integration at TCR loci".* ***2023, Blood, 141(19), pp. 2316–2329, doi: 10.1182/blood.2022017378. Commentary by Weijie Li in Blood***

5. Pais G, Spinozzi G*, **Cesana D***, Benedicenti F, Albertini A, Bernardo ME, Gentner B, Montini E, Calabria A. **equal contribution. "ISAnalytics enables longitudinal and high-throughput clonal tracking studies in Hematopoietic Stem Cell Gene Therapy applications".* ***Briefings in Bioinformatics, 2023, 24(1), doi:10.1093/bib/bbac551***

6. Ferrari S*, Jacob A,*, **Cesana D,***, Laugel M, Beretta S., Varesi A, Canarutto D, Albano L, Conti A., Calabria A., Vavassori V, Cipriani C., Castiello M.C., Unali G., Esposito S., Brombin C, Cugnata F., Adjali O., Ayuso E., Merelli

I., Villa A., Di Micco R., Kajaste-Rudnitski A, Montini E, Penaud-Budloo M., Luigi Naldini. **equal contribution.* *"Choice of Template Delivery Mitigates the Genotoxic Risk and Adverse Impact of Editing in Human Hematopoietic Stem Cells".* ***2022, Cell Stem Cells, Oct 6;29(10):1428-1444.e9. doi: 10.1016/j.stem.2022.09.001***

7. Del Core L., **Cesana D.**, Gallina P., Secanechia Y. N., Rudilosso L., Montini E., Wit E. J. C., Calabria A., and Grzegorczyk M. A. *"Normalization of clonal diversity in Gene Therapy studies using shape constrained splines"* ***2022, Scientific Reports 12(1),3836. doi: 10.1038/s41598-022-05837-0. PMID: 35264585***

8. Gentner B, Tucci F, Galimberti S, Fumagalli F, De Pellegrin M, Silvani P, Camesasca C, Pontesilli S, Darin S, Ciotti F, Sarzana M, Consiglieri G, Filisetti C, Forni G, Passerini L, Tomasoni D, **Cesana D**, Calabria A, Spinozzi G, Cicalese M, Calbi V, Migliavacca M, Barzaghi F, Ferrua F, Gallo V, Miglietta S, Zonari E, Cheruku P, Forni C, Facchini M, Corti A, Gabaldo M, Zancan S, Gasperini S, Rovelli A, Boelens JJ, Jones SA, Wynn R, Baldoli C, Montini E, Gregori S, Ciceri F, Valsecchi MG, la Marca G, Parini R, Naldini L, Aiuti A, Bernardo ME. *"Hematopoietic Stem- and Progenitor-Cell Gene Therapy for Hurler Syndrome"* **2021, N Engl J Med, Nov;18;385(21):1929-1940. doi: 10.1056/NEJMoa2106596. PMID: 34788506**

9. **Cesana D**, Calabria A, Rudilosso L, Gallina P, Benedicenti F, Spinozzi G, Schiroli G, Magnani A, Acquati S, Fumagalli F, Calbi V, Witzel M, Bushman FD, Cantore A, Genovese P, Klein C, Fischer A, Cavazzana M, Six E, Aiuti A, Naldini L, Montini E.*"Retrieval of vector integration sites from cell-free DNA".* **2021, Nat Med, Aug;27(8):1458-1470. doi: 10.1038/s41591-021-01389-4. PMID: 34140705**

10. **Cesana D[$]**, Santoni de Sio FR, Rudilosso L, Gallina P, Calabria A, Beretta S, Merelli I, Bruzzesi E, Passerini L, Nozza S, Vicenzi E, Poli G, Gregori S, Tambussi G, Montini E*. **[$]co-corresponding Author** *"HIV-1-mediated insertional activation of STAT5B and BACH2 trigger viral reservoir in T regulatory cells".* **2017, Nature Communications. Sep 8; 8(1):498, doi: 10.1038/s41467-017-00609-1.**

D. Past and Ongoing Research Support

(Complete the following table with the list of your projects, Add/delete rows if necessary.)

From To	Project Title	Funding Agency	Role in the project
03/2025 - 03/2030	Dissect the impact, safety and effectiveness of gene therapy at the whole organismal level by cell-free DNA signatures	European Research Council-Consolidator Grant	PI
03/2023 – 09/2025	cell-free DNA as a new biomarker for metachromatic leukodystrophy	ELA-foundation	Co- PI
2019 - 2022	Combining Patient-Derived Xenografts and Lentiviral Vector-Based Insertional Mutagenesis to Decipher Mechanisms of Leukemia Immune Evasion and Relapse	Italian Ministry of Health-Giovani Ricercatori	Co- PI
2018 - 2021	Improving the safety and long-term efficacy of hematopoietic stem cell based Gene Therapy and optimization of the treatment protocol through in vivo characterization of the stem cell proliferation stress during the hematopoietic reconstitution	Italian Ministry of Health-Giovani Ricercatori	Co- PI

2017 - 2020	Investigating insertional mutagenesis as a new mechanism of HIV-1 persistence in infected host	Italian Ministry of Health-Giovani Ricercatori	PI

E. Experience as a research supervisor

0 postdocs:

3 PhD students:

2022-2024 Elena Bruzzesi, second supervisor with Silvia Nozza (Dos), Ph.S student in Molecular Medicine at Università Vita-Salute San Raffaele, Milan

2022-present Carlo Cipriani, co-supervisor with Marco Masseroli, Ph.D student in Computer Science and Engineering, at Politecnico di Milano, Milan

2022-present Francesco Gazzo, co-supervisor with Marco Masseroli, Ph.D student in Computer Science and Engineering, at Politecnico di Milano, Milan

3 undergraduates:

2025-present Adriano A. Belli-Fernandez, Master degree in Pharmaceutical Biotechnology at Università degli Studi di Milano, Milan, Italy

2024-2025 Elisa Bonomi, Master degree in Bioinformatics for computational genomics at Università degli Studi di Milano - Politecnico di Milano, Milan, Italy

2015-2017 Elena Bruzzesi, co-supervisor with G. Tambussi, Master degree in Medicine at Università Vita-Salute San Raffaele, Milan, Italy